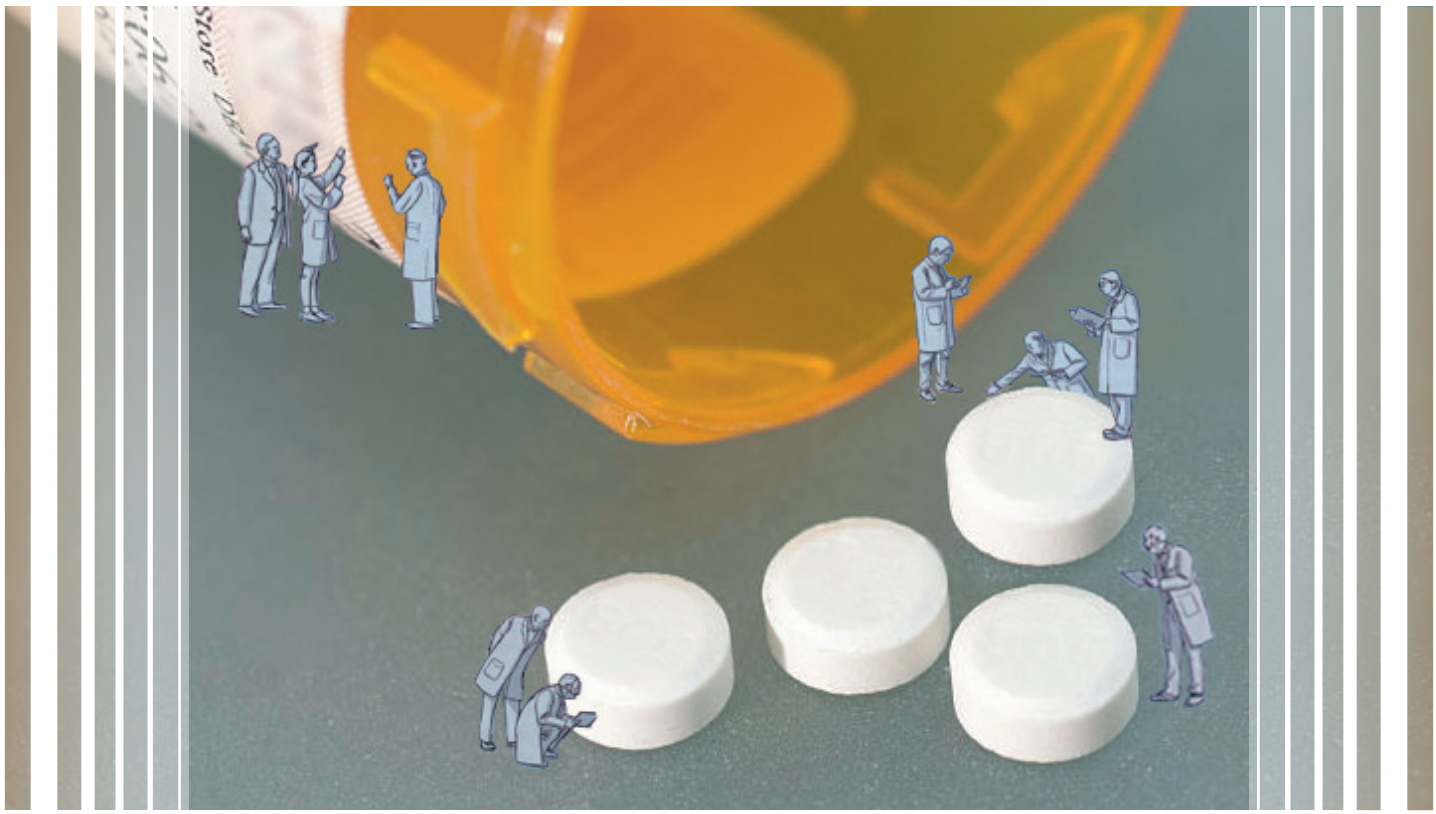
Seventh meeting of the Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy

Geneva, 26–27 February 2018



World Health Organization

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WHO/CDS/NTD/PCT/2018.06

Suggested citation. Seventh meeting of the Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy, Geneva, 26–27 February 2018. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at http://apps.who.int/iris.

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Printed in France.

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1. Introduction

Helminth control programmes based on preventive chemotherapy for the control of schistosomiasis, onchocerciasis, lymphatic filariasis and soil-transmitted helminthiasis are continuing to expand. In 2016, the global coverage of preventive chemotherapy reached 60%, with more than 1 billion individuals treated with anthelminthic medicines (albendazole, ivermectin, mebendazole and praziquantel,).

The expansion of preventive chemotherapy may pose a potential risk of triggering the development of anthelminthic resistance to these essential medicines and thereby jeopardize the long-term public health benefits of the interventions. Anthelmintic resistance is not yet a public health problem in human helminthiasis, but resistance is problematic in helminths of veterinary importance.

The Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy was established by the World Health Organization (WHO) in 2011 with the purpose of promoting:

- the establishment of a standard system for monitoring drug efficacy;
- the judicious use of anthelminthic medicines in order to sustain their efficacy and delay resistance; and
- the testing of alternative medicines or combinations of medicines should resistance emerge against the anthelminthics currently used in preventive chemotherapy programmes.

At the sixth meeting of the WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases (Geneva, 29–30 April 2013) it was recommended to merge the Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy with the Working Group on Monitoring & Evaluation so as to integrate monitoring of drug efficacy with overall monitoring and evaluation activities. Both working groups report to the Strategic and Technical Advisory Group on the progress of ongoing work, next steps and recommendations.

The seventh meeting of the Working Group on Monitoring of Neglected Tropical Diseases Drug Efficacy was held at WHO headquarters in Geneva, Switzerland on 26–27 February 2018. The meeting was chaired by Professor Josef Vercruysse. The rapporteurs were Dr Dora Buonfrate and Dr Antonio Montresor. The agenda is attached as Annex 1 and the list of participants as Annex 2.

2. Praziquantel

2.1 Background

In 2016, more than 80 million individuals were treated in preventive chemotherapy programmes, achieving a global coverage of the intervention in school-age children of 54%.

Praziquantel is the only medicine currently available for the treatment of schistosomiasis, yet its mode of action remains unknown. Other molecules have proven some efficacy, but they are either not available in large quantities or require further studies.

Reduced efficacy of praziquantel has not been documented in human infections, although the large number of individuals treated every year represents a concern for the future.

Morbidity in preschool children due to schistosome infection has been well documented, but preventive chemotherapy programmes targeting this age group are currently not implemented because the treatment of this group of children is expressly excluded by drug manufacturers.

2.2 Progress of ongoing work

The University of Texas Health Science Center has conducted in vitro laboratory tests to identify the genes responsible for resistance to praziquantel. A specific region in the parasite genome, which might host one or more genes responsible for reduced sensitivity to praziquantel, has been identified. The findings now need to be confirmed with further studies in the field.

Oxamniquine is a promising option for combination therapy, as it is already registered for the indication of schistosomiasis and has already been administered to millions of people, with no safety issues. However, it is effective only against *Schistosoma mansoni*.

Oxamniquine derivative molecules (e.g. CIDD 790) with efficacy also against *S. haematobium* and *S. japonicum* are under study at the University of Texas and other institutions. However, for these molecules to become available they must be registered as new compounds and a longer period of time will thus be required before they become available on the market.

In areas where schistosomiasis is endemic, animals (especially ruminants) are frequently infected by *Schistosoma* spp. In areas in which preventive chemotherapy interventions are implemented for the control of human schistosomiasis, human infection by hybrids originating from livestock is increasing (probably also as a result of a reduction of the number of human species of schistosomes).

Imperial College London has developed the first model of animal–human transmission for schistosomiasis. The model is intended to facilitate the evaluation of the role of livestock in human transmission and the impact of the possible interventions. Several aspects should be considered: (i) treating animals with praziquantel would reduce the source of the infection but would also increase the drug pressure on the parasite, reduce refugia and probably entail an increased risk of developing drug resistance; (ii) in some endemic countries, suboptimal treatment with praziquantel is given to sick animals and such misuse can promote the emergence of drug resistance; and (iii) hybrids could expand the host (snails) range and the species of animals possibly involved in transmission.

The Pediatric Praziquantel Consortium was founded in 2012 and has started working on paediatric formulations, namely an enantiomer L-PZQ and the racemate PZQ, both in the format of oral disintegrable